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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,769	08/09/2006	Christopher Iain Grainger	GJE-1080	8319

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EXAMINER	
KINSEY WHITE, NICOLE ERIN	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
02/02/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/580,769	GRAINGER, CHRISTOPHER IAIN	
	Examiner	Art Unit	
	NICOLE KINSEY WHITE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8-12 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,8-12 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 4, 2010 has been entered.

Withdrawn Rejections

The rejection of claims 1, 7 and 13-15 under 35 U.S.C. 102(b) as being anticipated by Bot et al. (WO 00/00215) as been withdrawn in view of applicant's amendments to the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-6, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bot et al. (WO 00/00215).

The claims are drawn to a method for producing a virus-containing, micro-particle dry powder, comprising the steps of: spray-drying a mixture of the virus and a stabilizing carbohydrate using an outlet temperature of 20°C to 40°C, where the stabilizing carbohydrate is trehalose, wherein the concentration of the carbohydrate if from 2% w/v to 70% w/v, and wherein the drying air flow rate is from 4.8L/sec to 8L/sec (claim 1), the atomization air flow rate is from 0.10 to 0.6L/sec (claim 14), and the virus is an envelope virus (claim 15). In addition, the feed rate of the spray dryer is from 0.05 to 2 g/min (claim 8), where the spray dryer nozzle-tip configuration is 1 bar 10L/sec to 3 bar 30L/sec (claim 9) or 1.5 bar 14L/sec (claim 10) or 3 bar 22L/sec (claim 11).

Bot et al. discloses a method for producing a microparticle dry powder for, *inter alia*, pulmonary administration comprising spray-drying a mixture of a bioactive agent (e.g., a virus such as live influenza) (see page 9, lines 24-28 and Example XIV) and a carbohydrate (e.g., trehalose or starch) (see page 24, lines 16-20 and Example XIV). Bot et al. further teaches that the outlet temperature can range from 40°C to 120°C depending on the composition of the feed and the desired particulate characteristics (see page 37, lines 16-18), the aspiration air flow can be 300 L/min (5 L/sec), the feed rate can be 3 mL/min to 15 mL/min, and the atomization air flow rate is between 25 L/min to 50 L/min (0.42 L/sec to 0.83 L/sec) (see pages 37-39). Bot et al. also teaches spray drying devices with nozzles.

Bot et al. does not disclose the specific carbohydrate concentrations recited in claims 1 and 4-6 or the specific feed rate and nozzle configurations recited in claims 8-11. However, it is obvious and well within the purview of one of ordinary skill in the art

to varying the concentration of carbohydrate or to select and/or vary certain aspects or parameters of the spray drying device, including operating conditions such as inlet and outlet temperature, feed rate, atomization pressure, flow rate of the drying air, and nozzle configuration as noted on page 39 (lines 3-5) of Bot et al. Bot et al. states that, operating conditions such as inlet and outlet temperature, feed rate, atomization pressure, flow rate of the drying air, and nozzle configuration can be adjusted in accordance with the manufacturer's guidelines in order to produce the required particle size, and production yield of the resulting dry microstructures. Thus, Bot et al. teaches that one can change certain variables to achieve different particle size and production yield.

Further, according to section 2144.05 of the MPEP, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art **unless there is evidence indicating such concentration or temperature is critical**. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.")

A particular parameter must first be recognized as a result-effective variable, i.e., a variable, which achieves a recognized result, before the determination of the optimum

or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In the instant application, the concentration of carbohydrate, feed rate and spray drying devices/nozzles used by Bot et al. produced a recognized result (i.e., a stable microparticle dry powder comprising virus and an excipient such as trehalose, as claimed by applicant). Therefore, determining other optimum or workable concentrations of carbohydrate, nozzle configurations and feed rates is routine experimentation.

Absent a showing of unexpected results, the concentrations of carbohydrates recited in claims 1 and 4-6 and the feed rate and nozzle configurations recited in claims 8-11 are obvious over Bot et al.

Response to Arguments

In the reply dated January 4, 2010, applicant argues that Bot et al. does not teach the claimed invention, in particular, Bot et al. does not teach a specific amount of trehalose and that Example XIV relates to the use of starch (not trehalose), which produced a low yield/viability. Applicant's arguments have been fully considered, but not found persuasive.

As stated above, Bot et al. teaches the use of carbohydrates and names specifically trehalose among other suitable carbohydrates for use in the spray-drying method. Thus, one of ordinary skill in the art can substitute any of the suitable carbohydrates listed by Bot et al. in the spray-drying method (e.g., Example XIV) and achieve the same result (a micro-particle dry powder).

As for the concentration of carbohydrate, as stated above, it is well within the purview of one of ordinary skill in the art to vary concentrations in an effort to optimize what is already taught. Bot et al. teaches a concentration of carbohydrate (starch) in Example XIV, which produced micro-particles of influenza by spray-drying. Using the established teachings of Bot et al., one of ordinary skill in the art can then vary the type of carbohydrate as well as the concentration of carbohydrate to optimize the product.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bot et al. (WO 00/00215) as applied to claim 1 above and further in view of LiCalsi et al. (Vaccine, 1999, 17:1796-1803).

The claim is drawn to a method for producing a micro-particle dry powder comprising a viral particle, wherein the stabilizing carbohydrate is trehalose and where the virus is measles virus.

The teachings of Bot et al. are outlined above. Bot et al. does not teach the use of the measles virus in the claimed method. However, LiCalsi et al. teaches the use of measles virus in dry powder preparations for vaccination via inhalation. LiCalsi et al. teaches that the dry powder vaccines can be formed by a variety of techniques including spray drying, precipitation from supercritical fluids, and jet milling or micronization (see page 1800, left column).

Therefore, it would have been obvious to one of ordinary skill in the art to use the method taught by Bot et al. to produce a measles virus dry powder vaccine. One would have been motivated to do so given the suggestion by LiCalsi et al. that a dry powder

measles vaccine is more stable than a lyophilized vaccine (see the Introduction and section 2.3). There would have been a reasonable expectation of success given the fact that Bot et al. discloses producing dry powder composition with viruses similar in size and structure to measles virus. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 4-6, 8-12 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sutton et al. (WO 97/36578) and further in view of Roser et al. (U.S. Patent No. 6,190,701) and LiCalsi et al. (Vaccine, 1999, 17:1796-1803).

The claims are drawn to a method for producing a micro-particle dry powder comprising a viral particle, comprising the steps of: spray-drying a mixture of the viral particle and a stabilizing carbohydrate, wherein the stabilizing carbohydrate is trehalose.

Sutton et al. discloses a method for producing a microparticle dry powder for, *inter alia*, pulmonary administration comprising spray-drying a mixture of a therapeutic agent (e.g., a retrovirus or herpes virus) (see page 5, lines 1-5 and Example 3) and an excipient (e.g., a carbohydrate such as glucose or sucrose) (see page 6, lines 5-10 and Example 3). The amount of carbohydrate is at least 50% weight of the mixture, and often at least 70% to 80% (see page 6, lines 16-18). The outlet temperature can range from 40°C to 150°C (see page 9, lines 21-22 and see Example 3 where an outlet temperature of 39.9°C was used), and the feed rate can be 0.75 g/min or 0.72 g/min (see Examples 1-3). Sutton et al. also discloses that the drying air pressure can range from 1×10^5 to 10×10^5 Pa (see page 7, lines 30-33), which is equivalent to 1 to 10

bars, and high levels of drying air (see page 10, lines 1-3). Sutton et al. also teaches spray drying devices with nozzles.

Sutton et al. does not teach the use of trehalose. However, Sutton et al. does teach that the excipient will usually be chosen on account of its ability to dilute/stabilize the therapeutic agent, and because of its wall-forming properties. It should be capable of formulation for spray-drying. Suitable excipients include carbohydrates (see page 6, lines 5-9). It is well known in the art that trehalose is a carbohydrate and is commonly used as a stabilizer during spray-drying as evidenced by Roser et al. Roser et al. teaches that as a sugar solution containing an active molecule is dried, it can either crystallize when the solubility limit of the sugar is reached, or can become a supersaturated syrup. The ability of the sugar to resist crystallization is a crucial property of a good stabilizer. Trehalose is good at this. Further drying progressively solidifies the syrup, which turns into a glass at a low residual water content. Chemical diffusion is negligible in a glass and therefore chemical reactions virtually cease. Since denaturation is a chemical change it cannot occur in the glass and the molecules are stabilized (see col. 2, lines 35-51).

Thus, it would have been obvious for one of ordinary skill in the art to substitute trehalose for sucrose (both are known stabilizers) and the results would have been predictable.

Sutton et al. also does not teach the carbohydrate concentration recited in claim 6, the nozzle configurations recited in claims 9-11 or the air flow rates of claim 14. Nonetheless, it is well within the purview of one of ordinary skill in the art to vary

concentrations and select and/or vary certain aspects or parameters of a spray drying device, including operating conditions such as inlet and outlet temperature, feed rate, atomization pressure, atomization air flow rate, flow rate of the drying air, and nozzle configuration.

Further, according to section 2144.05 of the MPEP, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.")

A particular parameter must first be recognized as a result-effective variable, i.e., a variable, which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In the instant application, the carbohydrate concentrations and spray drying devices/nozzles used by Sutton et al. produced a recognized result (i.e., a stable microparticle dry powder comprising virus and an excipient such as trehalose, as claimed by applicant). Therefore, determining

other optimum or workable carbohydrate concentrations and nozzle configurations is routine experimentation.

Absent a showing of unexpected results, the carbohydrate concentrations and nozzle configurations recited in the claims are obvious over Sutton et al.

Sutton et al. also does not teach the use of the measles virus in the claimed method. However, LiCalsi et al. teaches the use of measles virus in dry powder preparations for vaccination via inhalation. LiCalsi et al. teaches that the dry powder vaccines can be formed by a variety of techniques including spray drying, precipitation from supercritical fluids, and jet milling or micronization (see page 1800, left column).

Therefore, it would have been obvious to one of ordinary skill in the art to modify the method taught by Sutton et al. and include measles virus. One would have been motivated to do so given the suggestion by LiCalsi et al. that a dry powder measles vaccine is more stable than a lyophilized vaccine (see the Introduction and section 2.3). There would have been a reasonable expectation of success given the fact that Sutton et al. discloses producing dry powder composition with viruses similar in size and structure to measles virus. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

In the reply dated January 4, 2010, applicant argues that Sutton et al. teaches the use of sucrose (not trehalose) and a preferable outlet temperature of 70˚C. Applicant also argues that Sutton et al. does not teach a drying airflow rate of from 4.8

L/sec to 8 L/sec. All of applicant's arguments have been fully considered but are not found persuasive.

As noted above, Roser et al. provides the teaching for the use of trehalose as well as the motivation to use trehalose (see the discussion of Roser et al. above).

The temperature requirements have been fully addressed above. Sutton et al teaches 39.9 °C, which falls within applicant's range. Even if Sutton et al. teaches that higher temperatures are preferred, as argued by applicant, this does not establish that 39.9°C should not be used.

With regard to airflow rates, Sutton et al. teaches the use of "high levels" of drying air. Again, one of ordinary skill in the art, through routine experimentation, can vary drying air flow rates, to optimize the method of Sutton et al., which produces a recognizable result (e.g., a stable microparticle dry powder comprising virus and a carbohydrate such as trehalose). It is noted that applicant states that the present invention also uses a "high drying air flow rate" to produce a dry product (see page 6 last paragraph of applicant's remarks).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE KINSEY WHITE whose telephone number is (571)272-9943. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nicole Kinsey White/
Examiner, Art Unit 1648

/Stacy B Chen/
Primary Examiner, Art Unit 1648